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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/019,441	02/05/1998	MITCHELL E. REFF	012712-502	2038

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EXAMINER	
HUYNH, PHUONG N	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 05/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/019,441	Applicant(s) REFF ET AL.	
	Examiner Phuong Huynh	Art Unit 1644	

-- Th MAILING DATE of this communication appears on th cov r sheet with the correspond nc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *Three* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-70* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42-70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 42-70 are pending.

2. In view of the amendment filed 2/24/03, the following rejections remain.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 42-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling only for (1) a chimeric anti-human CD23 antibody wherein the variable light chain "consisting of" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "consisting of" the polypeptide encoded by SEQ ID NO: 2, and a human constant region selected from the group consisting of human gamma-1 and human gamma3 constant region, (2) a composition comprising an anti-human CD23 antibody mentioned above and a pharmaceutically acceptable carrier, (3) a chimeric anti-human CD23 antibody wherein the variable light domain "consisting of" the polypeptide encoded by SEQ I DNO: 3, the variable heavy domain consisting of the polypeptide encoded by SEQ ID NO: 4 and a human constant region selected from the group consisting of a human gamma-1 constant region and a human gamma-3 constant region, (4) a chimeric anti-human CD23 antibody wherein the variable light domain consisting of the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "consisting of" the polypeptide encoded by SEQ ID NO: 4 with the exception that the asparagines codon at position 75 is replaced with a lysine, (5) a composition comprising a chimeric anti-human CD23 antibody wherein the variable light domain "consisting of" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain consisting of the polypeptide encoded by SEQ ID NO: 4 and a human constant region selected from the group consisting of a human gamma-1 constant region and a human gamma-3 constant region and a pharmaceutical acceptable carrier, (6) a composition comprising a chimeric anti-human CD23 antibody wherein the variable light domain consisting of the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "consisting of" the polypeptide encoded by SEQ ID NO: 4 with the exception that the asparagines codon at position 75 is replaced with a lysine and a pharmaceutical acceptable carrier, (7) a composition

comprising an anti-human CD23 antibody a chimeric anti-human CD23 antibody wherein the variable light domain "consisting of" the polypeptide encoded by SEQ I DNO: 3, the variable heavy domain consisting of the polypeptide encoded by SE QI DNO: 4, a human gamma-1 constant region and a pharmaceutical acceptable carrier, (8) a composition comprising an anti-human CD23 antibody a chimeric anti-human CD23 antibody wherein the variable light domain "consisting of" the polypeptide encoded by SEQ I DNO: 3, the variable heavy domain consisting of the polypeptide encoded by SE QI DNO: 4, a human gamma-3 constant region and a pharmaceutical acceptable carrier, (9) a composition comprising a chimeric anti-human CD23 antibody wherein the variable light domain consisting of the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "consisting of" the polypeptide encoded by SEQ ID NO: 4 with the exception that the asparagines codon at position 75 is replaced with a lysine, a human gamma-1 constant region and a pharmaceutical acceptable carrier, and (10) a composition comprising a chimeric anti-human CD23 antibody wherein the variable light domain consisting of the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "consisting of" the polypeptide encoded by SEQ ID NO: 4 with the exception that the asparagines codon at position 75 is replaced with a lysine, a human gamma-3 constant region and a pharmaceutical acceptable carrier for inhibiting IL-4 induced IgE production in vitro, **does not** reasonably provide enablement for (1) *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "**comprising**" a human constant region selected from the group consisting of human gamma-1 and human gamma3 constant region, (2) *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "**comprising**" a human constant region wherein the human constant region is a human gamma-1 constant region, (3) *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "**comprising**" a human constant region wherein the human constant region is a human gamma-3 constant region, (4) *any* pharmaceutical composition containing *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "**comprising**" a human constant region selected from the group consisting of human gamma-1

and human gamma-3 constant region and a pharmaceutically acceptable carrier, (5) *any* pharmaceutical composition containing *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "comprising" a human constant region wherein the human constant region is a human gamma-1 constant region, and a pharmaceutically acceptable carrier, (6) *any* **pharmaceutical composition** containing *any* chimeric anti-human CD23 antibody mentioned above, (7) *any* chimeric anti-human CD23 antibody wherein the variable light domain "**comprises**" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ I DNO: 4 and a human constant region selected from the group consisting of a human gamma-1 constant region and a human gamma-3 constant region, (8) *any* chimeric anti-human CD23 antibody wherein the variable light domain "**comprises**" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 4 with the exception that the asparagines codon at position 75 is replaced with a lysine, (9) *any* chimeric anti-human CD23 antibody wherein the variable light domain "**comprises**" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ I DNO: 4 and a human constant region which "**comprises**" human gamma-1 constant region, (10) *any* chimeric anti-human CD23 antibody wherein the variable light domain "comprises" the polypeptide encoded by SEQ I DNO: 3, the variable heavy domain "comprises" the polypeptide encoded by SEQ I DNO: 4 and a human constant region which "**comprises**" human gamma-3 constant region, (11) *any* chimeric anti-human CD23 antibody wherein the variable light domain "**comprises**" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 4 with the exception that the asparagines codon at position 75 is replaced with a lysine "which comprises" a human gamma-3 constant region, and (12) *any* pharmaceutical composition comprising any anti-human CD23 antibody mentioned above for treating *any* diseases such as autoimmune diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in **scope** with these claims.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working

examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention. The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation.

The specification discloses only five murine anti-human CD23 monoclonal antibodies (5E8, 6G5, 2C8, B3B11 and 3G12) and six primate anti-human CD23 monoclonal antibodies (P5E8G4P, p5E8G1PN, p5E8G1, p5E8G1N, p6G5G1 and p6G5G4P) and these primatized antibodies contain human gamma-1 or human gamma-4 constant regions for inhibiting IgE production in vitro.

The specification does not provide sufficient guidance and working examples to enable one skilled in the art to make and use *any* chimeric anti-human CD23 antibody mentioned above that has the functional capacity to inhibit IgE, much less for treating any disease. The term "comprises" or "comprising" is open-ended. It expands the variable light chain domain, the variable heavy chain domain and the constant region, which are all fragments of the chimeric anti-human CD23 antibody, to include additional amino acid at either or both ends, and the corresponding polynucleotide encoding the additional amino acids. Without the specific amino acid residues (structure) and the corresponding polynucleotide, one skilled in the art would not be able to add such that the resulting antibody would still bind human CD23 and block IgE. It is well known in the art that a nucleic acid sequence is not sufficient to know the structure and/or function of the protein encoded by said nucleic acid sequence. It is well known in the art that a nucleic acid sequence is not sufficient to know the structure and/or function of the protein encoded by said nucleic acid sequence.

Skolnick *et al* teach that determining the sequence of a nucleic acid molecule does not provide sufficient information to obtain the structure of the protein. Further, the function of a protein cannot be determined simply by knowing the structure of a protein, as many proteins are multifunctional. Changes in nucleic acid sequence can, therefore, potentially result in changes in essential three-dimensional structures of the given protein, and consequently, it's function.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed amino acid and the corresponding polynucleotide, it is unpredictable which undisclosed variable light chain, variable heavy chain domain and constant domain will have the same binding specificity and function as

the chimeric anti-human CD23 antibody such as p5E8G1, p5E8G1N, and p6G5G1, in turn, would be useful for *any* purpose. Since the variable light chain and heavy chain domains are not enabled, the binding specificity of the claimed chimeric anti-human CD23 antibody is not enabled. It follows that the pharmaceutical composition comprising any chimeric anti-human CD23 is not enabled. Further, there is insufficient guidance as to the specific disease such as autoimmune disease could be treated using any chimeric anti-human CD23 antibody mentioned above.

Van Noort *et al* teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular). Given the indefinite number of undisclosed inflammatory autoimmune disease, it is unpredictable which undisclosed chimeric anti-human CD23 antibody would be useful for treating any autoimmune disease. Further, the Merck manual does not recognize the use of *any* chimeric anti-human CD23 for treating *any* inflammatory autoimmune disease such as rheumatoid arthritis (See page 420-421, in particular). Even if the chimeric anti-human CD23 antibody is use for inhibiting the production of IgE induced by IL-4, the in vivo data as shown in Figures 9 and 10 are not significantly different than the control (See error bars).

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In re wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), the decision of the court indicates that the more unpredictable the area is, the more specific enablement is necessary. In view of the quantity of experimentation necessary, the limited working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take an undue amount of experimentation for one skilled in the art to practice the claimed invention.

Applicants' arguments filed 2/24/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) the claimed invention is described in the specification, (2) the specification provides example showing how to introduce a mutation (substitution) into the amino acid sequence of one of the disclosed antibody polypeptide (gamma-4 constant region). (3) The present specification shows that heavy chain variable regions of both primate antibodies 5E8 and 6G5 bind effectively to CD23, whether they are attached to either monkey or human

hamma-1 or gamma-4 constant chains. (4) the Examiner's attention is directed to claims 1 of co-owned US Pat No 6,136,310 and 6,001,358 patents. While every application must be examined on its merits the recent allowance by USPTO of claims to antibodies using "comprising" language as shown in the above two examples, can regard as additional evidence that antibodies encompassed by such claims can be made and used by those skilled in the art without undue experimentation.

However, instant claim 42 recites a chimeric anti-human CD23 antibody wherein the variable light domain "comprises" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain comprises the polypeptide of SEQ ID NO: 2 and comprising a human constant region selected from the group consisting of human gamma-1 and human gamma-3 constant regions. The variable light **"domain"** and variable heavy "**domain**" are fragments of the light chain and the heavy chain of an antibody, respectively. Since variable light domain and variable heavy domain are fragments of an antibody, the term "comprising" is open-ended. It expands the "variable light domain" and "variable heavy domain" to include additional amino acids at either or both ends of said "variable light domain" and "variable heavy domain". Given the indefinite number of amino acid, the corresponding polynucleotide encoding said undisclosed amino acid to be added, there is insufficient guidance as to the undisclosed amino acids to be added and whether the resulting chimeric antibody would still bind to human CD23. Without the specific amino acid residues (structure) and the corresponding polynucleotide, one skilled in the art would not be able to add such that the resulting antibody would still bind human CD23 and block IgE. It is well known in the art that a nucleic acid sequence is not sufficient to know the structure and/or function of the protein encoded by said nucleic acid sequence. It is well known in the art that a nucleic acid sequence is not sufficient to know the structure and/or function of the protein encoded by said nucleic acid sequence. It is well known in the art that a nucleic acid sequence is not sufficient to know the structure and/or function of the protein encoded by said nucleic acid sequence.

Skolnick *et al* teach that determining the sequence of a nucleic acid molecule does not provide sufficient information to obtain the structure of the protein. Further, the function of a protein cannot be determined simply by knowing the structure of a protein, as many proteins are multifunctional. Changes in nucleic acid sequence can, therefore, potentially result in changes in essential three-dimensional structures of the given protein, and consequently, it's function.

Abaza *et al* teach that even a single amino acid substitution outside the antigenic site can exert drastic effects on the reactivity of a protein with monoclonal antibody against the site (See abstract, in particular). Given the indefinite number of undisclosed amino acid and the corresponding polynucleotide, it is unpredictable which undisclosed variable light chain, variable heavy chain domain and constant domain will have the same binding specificity and function as the chimeric anti-human CD23 antibody such as p5E8G1, p5E8G1N, and p6G5G1, in turn, would be useful for *any* purpose. Since the variable light chain and heavy chain domains are not enabled, the binding specificity of the claimed chimeric anti-human CD23 antibody is not enabled. It follows that the pharmaceutical composition comprising any chimeric anti-human CD23 is not enabled. Further, there is insufficient guidance as to the specific disease such as autoimmune disease could be treated using any chimeric anti-human CD23 antibody mentioned above.

Van Noort *et al* teach autoimmune diseases can be species and model-dependent (See entire document, pages 167-168, in particular). Given the indefinite number of undisclosed inflammatory autoimmune disease, it is unpredictable which undisclosed chimeric anti-human CD23 antibody would be useful for treating any autoimmune disease. Further, the Merck manual does not recognize the use of *any* chimeric anti-human CD23 for treating *any* inflammatory autoimmune disease such as rheumatoid arthritis (See page 420-421, in particular). Even if the chimeric anti-human CD23 antibody is use for inhibiting the production of IgE induced by IL-4, the in vivo data as shown in Figures 9 and 10 are not significantly different than the control (See error bars).

Even if the antibody in the pharmaceutical composition is limited to the specific chimeric antibody wherein the light chain comprises the polypeptide encoded by SEQ ID NO: 1, the heavy chain comprises SEQ ID NO: 2, the specification does not adequately teach how to effectively treat *any* disease or reach any therapeutic endpoint in humans by administering any pharmaceutical composition comprising any chimeric anti-human CD23. The specification does not teach how to extrapolate data obtained from in vitro or in vivo inhibition of IgE production to the development of effective in vivo human therapeutic compositions for treating *any* disease, commensurate in scope with the claimed invention. Therefore, it is not clear that the skilled artisan could predict the efficacy of the chimeric antibody exemplified in the specification or the breadth of claims. Given the indefinite number of undisclosed disease, undue experimentation would be required to practice the claimed pharmaceutical composition.

For these reasons, it would require undue experimentation of one skilled in the art to practice the claimed invention. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

5. Claims 42-70 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

The specification does not reasonably provide a **written description** of (1) *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "**comprising**" a human constant region selected from the group consisting of human gamma-1 and human gamma3 constant region, (2) *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "**comprising**" a human constant region wherein the human constant region is a human gamma-1 constant region, (3) *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "**comprising**" a human constant region wherein the human constant region is a human gamma-3 constant region, (4) *any* pharmaceutical composition containing *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "**comprising**" a human constant region selected from the group consisting of human gamma-1 and human gamma-3 constant region and a pharmaceutically acceptable carrier, (5) *any* pharmaceutical composition containing *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2, and "comprising" a human constant region wherein the human constant region is a human gamma-1 constant region, and a pharmaceutically acceptable carrier, (6) *any* **pharmaceutical composition** containing *any* chimeric anti-human CD23 antibody mentioned above, (7) *any* chimeric anti-human CD23 antibody wherein the variable light domain "**comprises**" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "**comprises**"

the polypeptide encoded by SEQ I DNO: 4 and a human constant region selected from the group consisting of a human gamma-1 constant region and a human gamma-3 constant region, (8) *any* chimeric anti-human CD23 antibody wherein the variable light domain "**comprises**" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 4 with the exception that the asparagines codon at position 75 is replaced with a lysine, (9) *any* chimeric anti-human CD23 antibody wherein the variable light domain "**comprises**" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ I DNO: 4 and a human constant region which "**comprises**" human gamma-1 constant region, (10) *any* chimeric anti-human CD23 antibody wherein the variable light domain "comprises" the polypeptide encoded by SEQ I DNO: 3, the variable heavy domain "comprises" the polypeptide encoded by SEQ I DNO: 4 and a human constant region which "**comprises**" human gamma-3 constant region, (11) *any* chimeric anti-human CD23 antibody wherein the variable light domain "**comprises**" the polypeptide encoded by SEQ ID NO: 3, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 4 with the exception that the asparagines codon at position 75 is replaced with a lysine "which comprises" a human gamma-3 constant region, and (12) *any* pharmaceutical composition comprising any anti-human CD23 antibody mentioned above for treating *any* diseases such as autoimmune diseases.

The specification discloses only five murine anti-human CD23 monoclonal antibodies (5E8, 6G5, 2C8, B3B11 and 3G12) and six primate anti-human CD23 monoclonal antibodies (P5E8G4P, p5E8G1PN, p5E8G1, p5E8G1N, p6G5G1 and p6G5G4P) and these primatized antibodies contain human gamma-1 or human gamma-4 constant regions for inhibiting IgE production in vitro.

With the exception of the specific a chimeric anti-human CD23 antibody, there is insufficient written description about the structure associated with function of *any* chimeric anti-human CD23 antibody wherein the variable light chain "**comprises**" the polypeptide encoded by SEQ ID NO: 1 or 3, the variable heavy domain "**comprises**" the polypeptide encoded by SEQ ID NO: 2 or 4, and "**comprising**" a human constant region selected from the group consisting of human gamma-1 and human gamma3 constant region. The term "comprises" or "comprising" is open-ended. It expands the variable light chain domain, the variable heavy chain domain and the constant region, which are all fragments of the chimeric anti-human CD23 antibody, to include additional amino acid at either or both ends, and the corresponding polynucleotide encoding the

additional amino acids. Further, the specification disclosed only six chimeric anti-human CD23 antibodies. Given the lack of a written description of *any* pharmaceutical composition comprising *any* chimeric anti-human CD23 for treating *any* disease, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus. *See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.*

Applicant is directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Applicants' arguments filed 2/24/03 have been fully considered but are not found persuasive.

Applicants' position is that (1) the claimed invention is described in the specification, (2) the specification provides example showing how to introduce a mutation (substitution) into the amino acid sequence of one of the disclosed antibody polypeptide (gamma-4 constant region). (3) The present specification shows that heavy chain variable regions of both primate antibodies 5E8 and 6G5 bind effectively to CD23, whether they are attached to either monkey or human hamma-1 or gamma-4 constant chains. (4) the Examiner's attention is directed to claims 1 of co-owned US Pat No 6,136,310 and 6,001,358 patents. While every application must be examined on its merits the recent allowance by USPTO of claims to antibodies using "comprising" language as shown in the above two examples, can regard as additional evidence that antibodies encompassed by such claims can be made and used by those skilled in the art without undue experimentation.

However, instant claim 42 recites a chimeric anti-human CD23 antibody wherein the variable light domain "comprises" the polypeptide encoded by SEQ ID NO: 1, the variable heavy domain comprises the polypeptide of SEQ ID NO: 2 and comprising a human constant region selected from the group consisting of human gamma-1 and human gamma-3 constant regions. The variable light "**domain**" and variable heavy "domain" are fragments of the light chain and the heavy chain of an antibody, respectively. Since "variable light domain" and "variable heavy domain" are fragments of an antibody, the term "comprising" is open-ended. It expands the "variable light domain" and "variable heavy domain" to include additional amino acids at either or both ends of said "variable light domain" and "variable heavy domain". Given the indefinite number of undisclosed amino acid to be added, and the corresponding polynucleotide encoding

said undisclosed amino acid, there is inadequate written description about the undisclosed amino acid and whether the resulting chimeric antibody would still bind to human CD23, let alone inhibiting IgE in vivo for treating *any* disease.

6. The following new ground of rejection is necessitated by the amendment filed 2/24/03.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 49, 55 and 65 are rejected under 35 U.S.C. 112, first paragraph, containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

The "asparagines codon at position 75 is replaced with a lysine" in Claim 49 represents a departure from the specification and the claims as originally filed. Applicant's sequence listing of SEQ ID NO: 4 has glutamine at said position, not asparagines. Further, Applicants have not pointed out the support for said phrase.

9. Claims 42-70 appear to be free of prior art.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, THIS ACTION IS MADE FINAL. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to "Neon" Phuong Huynh whose telephone number is (703) 308-4844. The examiner can normally be reached Monday through Friday from 9:00 am to 6:00 p.m. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

13. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-7401.

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May 19, 2003

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